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CASE REPORT

An unusual case of subclinical diffuse glucagonoma coexisting with two nodules in the pancreas: Characteristic features on computed tomography

N. Azemoto[a], T. Kumagi[b,*], T. Yokota[c], T. Kuroda[b], M. Koizumi[b], H. Yamanishi[b], Y. Soga[d], S. Furukawa[b], M. Abe[b], Y. Ikeda[a], Y. Hiasa[b], B. Matsuura[b], J. Watanabe[e], F. Kushihata[e], M. Onji[b]

[a] *Endoscopy Center, Ehime University Hospital, Shitsukawa, Toon, Ehime, Japan*
[b] *Department of Gastroenterology and Metabology, Ehime University Graduate School of Medicine, Toon, Ehime, Japan*
[c] *Center for Liver-Biliary-Pancreatic Disease, Matsuyama Red Cross Hospital, Matsuyama, Ehime, Japan*
[d] *Pathology Division, Ehime University Hospital, Shitsukawa, Toon, Ehime, Japan*
[e] *Hepato-biliary-pancreatic Surgery and Transplantation, Ehime University Graduate School of Medicine, Toon, Japan*

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Summary A lesion was discovered in the tail of the pancreas by ultrasonography performed during a health checkup for a 59-year-old Japanese man. Abdominal contrast-enhanced computed tomography (CE-CT) revealed strong enhancement in a 4-cm tumor in the pancreatic tail and in a 1-cm tumor in the pancreatic body. Serum glucagon levels were elevated to 54,405 pg/mL and a preoperative diagnosis of glucagonoma was made. The pancreatic tail and spleen were resected en bloc, along with a protruding tumor in the pancreatic body. However, histopathological evaluation revealed diffuse glucagonoma throughout the pancreas. When we retrospectively reviewed abdominal CE-CT after the operation, the entire pancreas was seen to be enlarged and diffusely enhanced by strong spots. Immunohistochemical examination using anti-CD31 demonstrated rich microvessels in two solid glucagonomas as well as microglucagonoma throughout the entire pancreas, indicating hypervascularity. Enlarged pancreas and diffuse enhancement of the pancreas by strong spots may be characteristic features of diffuse glucagonoma on abdominal CE-CT.

Introduction

Glucagonoma was initially reported in 1942 by Becker et al. [1]. This rare tumor accounts for only 1 to 7% of all pancreatic endocrine tumors [2,3]. The mean age at onset was

* Corresponding author. Tel.: +81 89 960 5308; fax: +81 89 960 5310.
E-mail address: terukuma@m.ehime-u.ac.jp (T. Kumagi).

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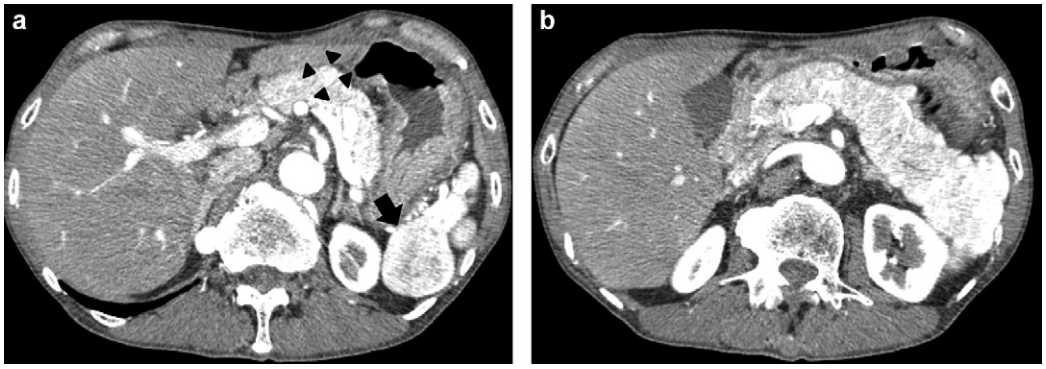

Figure 1 (a, b): abdominal contrast-enhanced computed tomography; (a): the 4-cm and 1-cm tumors in the pancreatic tail (arrows) and body (arrowhead), respectively, with distinct borders show enhancement in the early phase; (a, b): the entire pancreas was enlarged and showed strongly enhancing spots on contrast-enhanced computed tomography.

initially suggested to be 52.5 years, with a slight prediction towards females [4], but the most recent series finds an even distribution between males and females [5]. Glucagonomas are derived from pancreatic islet α cells, and around 50% develop in the pancreatic tail. The size of the tumor varies, with a reported average diameter of 6.4 cm [4]. These tumors secrete glucagon, resulting in systemic symptoms including dermatitis (necrolytic migratory erythema), diabetes, depression, deep venous thrombosis, anemia, weight loss, abdominal pain and diarrhea [6]. Although to apply surgical resection in all patients with glucagonoma is controversial, it should be considered since malignant potential of glucagonoma is between 52 to 61%, with the liver followed by lymph nodes being the most commonly encountered distant metastatic cites [2,7].

Most glucagonomas are diagnosed as solitary tumors, and clinical features of diffuse glucagonoma in detail have been reported in only three cases to date [8—10]. We present herein a case of diffuse glucagonoma throughout the entire pancreas (coexisting with two distinct solid tumors) that displayed characteristic features on abdominal contrast-enhanced computed tomography (CE-CT).

Case report

Patient

A lesion in the tail of the pancreas was discovered on ultrasonography performed during a health checkup in November 2007 for a 59-year-old Japanese man. Upon referral to our hospital in December 2007, he was asymptomatic and showed no abdominal pain. His family history was negative for pancreatic tumors. He did not smoke, but consumed about 20 g/day of alcohol.

Physical examination on admission revealed no palpable abdominal mass. Laboratory tests showed no abnormalities in levels of hepatobiliary enzymes. An OGTT yielded normal results, but early insulin secretion was impaired, with an insulinogenic index of 0.25 (normal insulinogenic index, > 0.4). The result of a pancreatic functional diagnostic test was low at 33.7%. Serum glucagon level was elevated to 54,405 pg/mL, although the level of total amino acids was as high as 6,332 nmol/mL. The levels of tumor markers, including carcinoembryonic antigen and carbohydrate antigen 19-9, were within normal limits.

Imaging studies

Abdominal ultrasonography and endoscopic ultrasonography showed a 4-cm tumor in the pancreatic tail. The tumor was hypoechoic, and had distinct borders. In the pancreatic body, a 1-cm hypoechoic tumor was observed. These tumors showed strong enhancement at an early stage on abdominal CE-CT (Fig. 1a). Endoscopic retrograde cholangiopancreatography showed no tumor-related narrowing, compression, or deviation of the main pancreatic duct. Subsequent ^{18}F-fluorodeoxyglucose positron emission tomography revealed slightly localized uptake of ^{18}F-fluorodeoxyglucose in the pancreatic tail only (maximum standardized uptake value: 2.95), not in the tumor in the pancreatic body. MRI of the head did not show any abnormalities, including pituitary tumor. Retrospective review of abdominal CE-CT after surgery revealed enlargement of the entire pancreas with diffuse enhancement in strong spots (Fig. 1a, b).

Findings at surgery

The pancreatic tail and spleen were resected en bloc, along with the protruding tumor in the pancreatic body. Visual inspection of the resected specimens showed single solid tumors in the pancreatic tail (3.5×3.5 cm) and body (1.2×1.0 cm) with distinct borders, with yellowish-white coloration and hard elastic consistency, and without invasion into surrounding tissue.

Histopathological examination

The two solid tumors that were apparent upon imaging showed typical features of neuroendocrine neoplasms, with distinct borders, eosinophilic cytoplasm, and lobulated nodules with funicular and ribbon-like arrangements. No nuclear division was evident. Immunohistochemical investigation revealed positive staining for synaptophisin, chromogranin A and glucagon, but negative staining for insulin, pancreatic polypeptide and gastrin. Ki-67 labeling was 5% in these